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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,962	12/31/2003	Chandrika Govardhan	ALTUS-4	2164
1473	7590	12/26/2007	EXAMINER	
ROPER & GRAY LLP			KIM, ALEXANDER D	
PATENT DOCKETING 39/361				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

**Application No.**

10/749,962

**Applicant(s)**

GOVARDHAN ET AL.

**Examiner**

Alexander D. Kim

**Art Unit**

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 03 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 4,7-10 and 17-65 is/are pending in the application.
- 4a) Of the above claim(s) 23-59 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4,7-10, 17-22 and 60-65 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)              |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____   |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application    |
| Paper No(s)/Mail Date _____  | 6) <input checked="" type="checkbox"/> Other: <u>NCBI AAA72260</u> . |

***Application Status***

***Continued Examination Under 37 CFR 1.114***

1. The art unit location of your application and/or examiner has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1656, Examiner Alexander Kim.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/06/2007 has been entered.

Applicants' amendment canceling Claims 1-3, 5-6 and 11-16; amending Claims 4, 7, 8-9, 17, 22 and 60-65 in the paper of 10/03/2007 is acknowledged. Claims 4, 7-10 and 17-65 are pending in the instant Office action. Claims 23-59 are withdrawn.

Thus, Claims 4, 7-10, 17-22 and 60-65 will be examined herein.

***New-Claims Objections***

3. Claims 62, 64 and 65 are objected for the following informality:

(a) Claim 62 recites "with.". It should be ---with a polyarginine.---

(b) Claims 64 and 65 objected to under 37 CFR 1.75(c) as being in improper form because Claims 60 to 63 or 64 are multiple dependent claims. See MPEP § 608.01(n). Accordingly, the claims 64 and 65 have not been further treated on the merits.

(c) Claim 64 recite "4, 7. 8, 9". It should be ---4, 7, 8, 9---, a comma instead of period after the number 7. Appropriate correction is required.

***Withdrawn-Claim Rejections - 35 USC § 112 – 1<sup>st</sup>***

4. The previous rejection of Claims 4, 7-10, 17-22 and 62-65 under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants' amendment.

5. The previous rejection of Claims 4, 7-10, 17-22 and 62-65 under 35 U.S.C. 112, first paragraph, written description, is withdrawn by virtue of Applicants' amendment.

***Double Patenting***

6. The previous provisional rejection of Claim 4 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 7, 9 and 10 of copending Application No. 11/169,956 (US 2006/0008532) is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that filing a Terminal Disclaimer is premature because neither claims are allowed.

However, two applications are still pending and the instant rejection is maintained.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 4, 7-10, 17, 19, 22 and 60-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Sorensen et al. (1998, US Patent 5,849,700).

Claims 4, 7-10, 17, 19, 22 and 60-65 are drawn to a polyarginine containing crystal of human growth hormone (hGH), wherein said hGH is the 191 amino acid sequence of native hGH, wherein the crystal is characterized by the recited limitations in Claims 7, 8, 9.

Sorensen et al. teach a crystal of human growth hormone (hGH) in the Example 4 (column 13) which consists of the 191 amino acid sequence because "Human growth hormone consists of 191 amino acids" (see column 1, lines 20-21). As shown in the hGH sequence (see NCBI AAA72260 in the attachment), the sequence of hGH contains many arginine residues and meets the limitation of a polyarginine containing crystal of hGH. Thus, the hGH crystal of Sorensen et al. meets the limitations of Claim 4.

The hGH crystal of Sorensen et al. is considered to have said characteristics of Claims 7-9 as evidenced by the instant disclosure of pharmacokinetic parameters in applicants' Table 6, in Example 16, page 54-56. Those recited limitations after the "wherein the crystal" clause do not appear to be associated with a particular structure or component of the claimed crystal and have been considered accordingly. Said "limitations" are considered inherent characteristics of the crystal of Sorensen et al. based upon the structure of the crystal. This is evidenced because claimed crystal is of human growth hormone, and based on the rat model as shown in Example 16, the crystal would have the same characteristics when said crystal is administered to a human. Thus, the crystal of Sorensen et al. meets the limitation of Claim 10.

Sorensen et al. also teach a composition comprising said crystal (1.3 mg/ml) with Benzyl alcohol in Example 7, column 17; thus, meeting the limitation of Claims 17, 19 and 22.

The crystal of Sorensen et al. also meets the limitation of Claims 60-63 and 65 because recited "the polyarginine containing crystal" of hGH reads on a multiple arginine residues in hGH crystal. Sorensen et al. also teach a pharmaceutical composition of said hGH crystal with sodium cation in the Example 9, column 17; thus, meeting the limitation of Claim 64.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 4, 7-10, 17-22 and 60-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen et al. (1998, US Patent 5,849,700) as evidenced by DeFelippis et al. (1998, J. Pharm. Sci., vol. 87, pages 170-176).

Sorensen et al. teach a crystal of human growth hormone (hGH) in the Example 4 (column 13) which consists of the 191 amino acid sequence because "Human growth hormone consists of 191 amino acids" (see column 1, lines 20-21). As shown in the hGH sequence (see NCBI AAA72260 in the attachment), the sequence of hGH contains many arginine residues and meets the limitation of a polyarginine containing crystal of hGH. Thus, the hGH crystal of Sorensen et al. meets the limitations of Claim 4.

The hGH crystal of Sorensen et al. is considered to have said characteristics of Claims 7-9 as evidenced by the instant disclosure of pharmacokinetic parameters in applicants' Table 6, in Example 16, page 54-56. Those recited limitations after the "wherein the crystal" clause do not appear to be associated with a particular structure or component of the claimed crystal and have been considered accordingly. Said "limitations" are considered inherent characteristics of the crystal of Sorensen et al. based upon the structure of the crystal. This is evidenced because claimed crystal is of human growth hormone, and based on the rat model as shown in Example 16, the crystal would have the same characteristics when said crystal is administered to a human. Thus, the crystal of Sorensen et al. meets the limitation of Claim 10.

Sorensen et al. also teach a composition comprising said crystal (1.3 mg/ml) with Benzyl alcohol in Example 7, column 17; thus, meeting the limitation of Claims 17, 19 and 22.

The crystal of Sorensen et al. also meets the limitation of Claims 60-63 and 65 because recited "the polyarginine containing crystal" of hGH reads on a multiple arginine residues in hGH crystal. Sorensen et al. also teach a pharmaceutical composition of said hGH crystal with sodium cation in the Example 9, column 17; thus, meeting the limitation of Claim 64.

Sorensen et al. do not teach limitation of excipient, e.g., protamine, (Claims 20-21) and/or said excipient having a molar ratio of hGH: excipient of 1:10 to 1:0.125 (Claim 18).

DeFelippis et al. disclose the protamine suspension of LysPro (human insulin analogue) having "8:1 molar ratio" (equivalent to 1:0.125) of LysPro to protamine (see bottom of left column, page 173 for pharmaceutical preparations of insulin.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the polyarginine containing hGH crystal of Sorensen et al. and a protamine excipient, with a concentration to have 8:1 molar ratio of the polyarginine containing hGH to protamine excipient as taught by DeFelippis et al. because the protamine is the most commonly used intermediate-acting suspension preparation (see bottom of left column, page 170). One would have been motivated to add protamine excipient into said hGH crystalline suspension in order to



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prolong a pharmaceutical composition in patients and increase the duration of its action  
(see top of right column, page 170) for making hGH intermediate-acting suspension.

Thus, the invention taken as a whole is *prima facie* obvious.

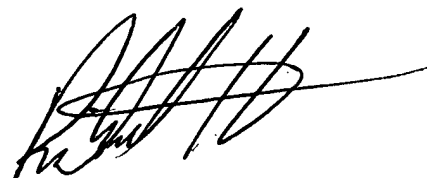
**Conclusion**

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 11AM-7:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim  
13 December 2007

A handwritten signature in black ink, appearing to read 'Richard Hutson', with a long horizontal stroke extending to the right.

**RICHARD HUTSON, PH.D.  
PRIMARY EXAMINER**